The identification of a donor has always limited the extent of allo HSCT. Recently it has been shown that a haploidentical donor could be a valid option to perform allo HSCT given adapted immunosuppression is used. Notably the use of PT-HDCy, after T-replete HSCT following reduced intensity (RIC) or non-myeloablative (NMAC) conditioning, has been associated with promising results. However little data exist concerning elderly population when this population is characterized by a lack of HLA matched sibling and a higher incidence of severe GVHD and non-relapse mortality.

Using this strategy we transplanted 31 patients over the age of 55 years between 2010 and 2014 and compare their outcome with patients of the same age transplanted in the same period from a MRD or UD.

70% of the patients in haplo group were prepared with Flu-TBI 2gy (NMAC) (30% received Fludarabine-Busilvex based regimen without ATG) while all patients in other groups received the same RIC (Fludarabine (150 mg/m^2) Busilvex (2 days) rabbit ATG (2 days)). Patients in haplo group received post graft immunosuppression with PT-HDCy (50 mg/kg on D 3 and 4) followed with CSA and MMF while patients in other groups received either CSA starting on D1.

Patients in the haplo group have a trend presenting higher comorbidities and more severe diseases (Table). A single graft failure related to donor anti-HLA antibodies were noted in haplo group. Median time to 0.5x10^9 ANC and 20x10^{9}platelets were respectively 21 (14-32) and 28 (14-52) days after haplo HSCT. Haplo and MRD HSCT patients presented with a similar NRM lower than UD patients while Haplo patients present a relapse rate intermediate between MRD and UD (table). Overall outcome after haplo do not differ from MRD transplant. There is a trend for better PFS after Haplo HSCT as compared with UD transplant (62% vs.41%; P=0,14) (Figure 1). Progression-free and severe cGVHD-free survival was significantly better after haplo HSCT (62% vs. 35%; p=0.03) (Figure 2).

We conclude that T-replete Haplo HSCT after RIC and followed by PT-HDCy is associated with promising results notably as compared with UD HSCT. The low rate of severe aGVHD and cGVHD are likely to conduct to lower complications and better quality of life. The reduction of donor search duration and the absence of graft acquisition fees represent potential additional benefits. In this perspective, the place of Haplo HSCT in older patients should now be prospectively addressed.

388

Presentation and Outcome of Zap 70 Deficiency

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ZAP70 (zeta-associated protein of 70 KDa) deficiency is a fatal form of combined immunodeficiency that can be cured with hematopoietic stem cell transplantation (HSCT). The normal number of thymocytes, polyclonal CD3$^+$ T cells and B cells may require special considerations in choosing the most effective regimen of conditioning and the type of HSCT. We analyzed presentation and outcome of patients with ZAP70 deficiency who received various modalities of stem cell transplantation.

Data on 19 patients with ZAP70 deficiency were examined, of whom 16 underwent HSCT in 7 different counties. HSCT was performed by using different sources of donor stem cells as well as various conditioning regimens.

Most patients presented with typical repeated microbial and fungal infections; one patient presented with lymphoma. Close family members appear to have a high frequency of autoimmunity. Sixteen of nineteen patients were treated with HSCT. Nine patients received a MRD and 8/9 survived, four patients had MUD transplants and all survived and 3 had a MMRD transplant of which only one survived. Immune reconstitution was complete and durable in patients who received myeloablative conditioning. Lack of conditioning failed in two patients and resulted in partial immune reconstitution in the other patients.

Based on these data, we conclude that carriers of monoallelic mutations in ZAP70 may be susceptible to autoimmunity. HLA matched donor and myeloablative conditioning result in superior outcome and long-term robust immune reconstitution.

389

A Multicenter Phase I/II Study of Relapse Prophylaxis with Nilotinib after Hematopoietic Cell Transplantation (HCT) for High-Risk Philadelphia Chromosome-Positive (Ph+) Leukemias

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Background: In a previous study, we showed that relapse prophylaxis with imatinib (IM) is feasible early after allogeneic HCT for treatment of Ph+ leukemia [Carpenter et al, Blood 2007;109:2791]. The goal of the current study was to ask whether nilotinib (NIL) might address IM resistance (IR) or intolerance (IT) because IR leukemia might be sensitive to NIL. Previous non-HCT trials have shown that NIL and IM have comparable hematopoietic toxicity, but the incidence of edema and gastrointestinal toxicity is less with NIL than with IM.